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Registration Decision

RD2014-08

Bacillus subtilis **strain GB03**

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Registration Decision for *Bacillus subtilis* strain GB03

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of *Bacillus subtilis* GB03 Technical Fungicide and the associated end-use products, Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide, containing the technical grade active ingredient *Bacillus subtilis* strain GB03, for use as seed treatments to suppress seed and root diseases caused by *Fusarium* spp. and *Rhizoctonia solani* on canola, mustard (oilseed and condiment), rapeseed, and legume vegetables including soybeans.

An evaluation of available scientific information found that, under the approved conditions of use, the products have value and do not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document¹ Proposed Registration Decision PRD2013-14, *Bacillus subtilis* strain GB03. This Registration Decision² describes this stage of the PMRA's regulatory process for *Bacillus subtilis* strain GB03 and summarizes the Agency's decision and the reasons for it. The PMRA received no comments on PRD2013-14. This decision is consistent with the proposed registration decision stated in PRD2013-14.

For more details on the information presented in this Registration Decision, please refer to the PRD2013-14, which contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable³ if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value⁴ when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

¹ "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

² "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

³ "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

⁴ "Value" as defined by subsection 2(1) of *Pest Control Products Act* "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What is *Bacillus subtilis* strain GB03?

Bacillus subtilis strain GB03 is a bacterium that is used as a microbial pest-control agent to suppress damping-off and root rot on canola, rapeseed and mustard (oilseed and condiment); and suppress seedling blight and root rot on legume vegetables including soybeans. *Bacillus subtilis* is a soil bacterium that is distributed globally, and commonly recovered from water, soil, air and decomposing plant residues. Strain GB03 of *B. subtilis* was originally isolated from healthy foliage of Douglas fir in Australia.

Bacillus subtilis strain GB03 is a root colonizer that directly competes with potential root pathogens for nutrients and space at the surface of roots and by producing antifungal agents such as iturins. *Bacillus subtilis* strain GB03 also reduces disease by inducing the plant's natural defense mechanisms, a process called induced systemic resistance.

Health Considerations

Can Approved Uses of *Bacillus subtilis* strain GB03 Affect Human Health?

***Bacillus subtilis* strain GB03 is unlikely to affect your health when Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide are used according to the label directions.**

People could be exposed to *B. subtilis* strain GB03 when handling and applying Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide. When assessing health risks, several key factors are considered:

- the micro-organism's biological properties (for example, production of toxic byproducts);
- reports of any adverse incidents;
- its potential to cause disease or toxicity as determined in toxicological studies; and
- the level to which people may be exposed relative to exposures already encountered in nature to other isolates of this micro-organism.

Toxicological studies in laboratory animals describe potential health effects from large doses in order to identify any potential pathogenicity, infectivity and toxicity concerns. When spores of *B. subtilis* strain GB03 were tested on laboratory animals, there were no signs that it caused any significant toxicity or disease.

Residues in Water and Food

Dietary risks from food and water are not of concern.

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine whether the consumption of the maximum amount of residues, that are expected to remain on food products when a pesticide is used according to label directions, will not be a concern to human health. This maximum amount of residues expected is then legally established as a Maximum Residue Limit (MRL) under the *Pest Control Products Act* for the purposes of the adulteration provision of the *Food and Drugs Act*. Health Canada sets science-based MRLs to ensure that the food Canadians eat is safe.

Bacillus subtilis strain GB03 is an ubiquitous bacterium that is commonly found in soil. When *B. subtilis* strain GB03 was administered orally to rats, no signs of toxicity or disease were observed, and no metabolites of toxicological significance have been shown to be produced by this strain of *B. subtilis*. Although some strains of *B. subtilis* have been isolated from food samples implicated in food poisoning, these strains demonstrated the ability to produce a highly heat-stable toxin that may be similar to a toxin produced by *Bacillus cereus*, a known food-borne pathogenic micro-organism. *Bacillus subtilis* strain GB03 is not reported to produce this toxin. Also, no such effects were reported for this micro-organism in the United States where it has been registered since 1992. Therefore the establishment of a MRL is not required for *B. subtilis* strain GB03. As well, the likelihood of residues contaminating drinking water supplies is negligible to non-existent. Consequently, dietary risks are minimal to non-existent.

Occupational Risks from Handling Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide

Occupational risks are not of concern when Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide are used according to label directions, which include protective measures.

Workers handling Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide can come into direct contact with *B. subtilis* strain GB03 on the skin, in the eyes or by inhalation. For this reason, the product label will specify that workers exposed to the end-use product must wear waterproof gloves, long-sleeved shirts, long pants, goggles, a NIOSH-approved respirator (with any N-95, P-95, R-95 or HE filter for biological products), and shoes plus socks.

For the bystander, exposure is expected to be much less than that of handlers and mixer/loaders and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When *Bacillus subtilis* strain GB03 is Introduced into the Environment?

Information available in the published literature on the environmental fate of *B. subtilis* strain GB03 suggests that, as a soil micro-organism, it is likely that *B. subtilis* strain GB03 could survive in soil under suitable environmental conditions (i.e. type of soil, moisture, acidity levels, and temperature) at elevated levels. However, the populations of *B. subtilis* strain GB03 should return to naturally occurring levels over time.

Studies were conducted to determine the effects of *B. subtilis* strain GB03 on birds, and terrestrial plants. These studies showed that *B. subtilis* strain GB03 was not toxic or pathogenic to birds and terrestrial plants. Waivers for avian pulmonary testing, wild mammals, arthropods and non-arthropod invertebrates toxicity testing as well as for freshwater fish, estuarine and marine fish, aquatic arthropods, and aquatic plants were deemed acceptable to address the remaining environmental toxicological requirements. The rationales were based on the ubiquitous nature of *B. subtilis* in both soil and water whose level in the terrestrial and aquatic environment will not significantly increase as a result of the use of Kodiak Concentrate Fungicide and Kodiak Flowable Fungicide as seed treatments; the toxicity profile of *B. subtilis* strain GB03 from laboratory animal studies; and a review of published literature which indicated a few reports of adverse effects to terrestrial organisms, and a lack of adverse effects to aquatic organisms from natural populations of *B. subtilis*.

In published literature, other strains of *B. subtilis* have been reported to cause infections in mammals, terrestrial insects and plants. However, these reports were few in number considering the large amount of published literature on this micro-organism. Furthermore, these reports involved unusual strains, or select strains, of *B. subtilis* for which their ability to cause disease was not thoroughly investigated. There are no reports with *B. subtilis* strain GB03 in non-target organisms except for the intended pest.

Value Considerations

What Is the Value of Kodiak Flowable Fungicide and Kodiak Concentrate Fungicides?

***Bacillus subtilis* strain GB03, the active ingredient in Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide, suppresses certain seedling and root diseases on canola, rapeseed, mustard (oilseed and condiment) and legume vegetables including soybeans.**

Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide, containing 5.0×10^{10} colony forming units (CFU)/mL or 5.5×10^{10} CFU/g *Bacillus subtilis* strain GB03, are products formulated as seed treatments to suppress seedling and root diseases caused by *Fusarium* spp. and *Rhizoctonia solani* on canola, rapeseed, mustard (oilseed and condiment), and legume vegetables including soybeans. Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide provide additional alternatives to disease management options for these diseases both in conventional agriculture as well as organic farming. When the Flowable Fungicide and Kodiak Concentrate Fungicide are used with a chemical seed treatment, the combination also contributes to resistance management by different modes of action.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

In individuals exposed to large quantities of Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide, respiratory and dermal sensitivity could possibly develop upon repeated exposure to the product since all micro-organisms, including *B. subtilis* strain GB03, contain substances that are potential sensitizers. Therefore, anyone handling or applying Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide must wear waterproof gloves, long-sleeved shirts, long pants, a NIOSH-approved respirator (with any N-95, P-95, R-95 or HE filter for biological products), and shoes plus socks. Due to the irritation potential identified for Kodiak Flowable Fungicide and Kodiak Concentrate Fungicide, workers and handlers are also required to wear eye goggles. Also, the signal words, "POTENTIAL SENSITIZER" and "WARNING-EYE and SKIN IRRITANT" on the principal display panel and precautionary statements, "Causes eye and skin irritation. DO NOT get in eyes or on skin" and "May cause sensitization" are required on the secondary display panel of the label for Kodiak Concentrate Fungicide. The signal words, "POTENTIAL SENSITIZER" and "CAUTION-EYE and WARNING - SKIN IRRITANT" on the principal display panel and precautionary statements, "May irritate eyes. Avoid contact with eyes. Causes skin irritation. DO NOT get on skin" and "May cause sensitization" are required on the secondary display panel of the label for Kodiak Flowable Fungicide.

Environment

The end-use product labels will include environmental precaution statements that prevent the contamination of aquatic systems from the use of Kodiak Concentrate Fungicide and Kodiak Flowable Fungicide.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2013-14, *Bacillus subtilis* strain GB03), are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection⁵ regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision, healthcanada.gc.ca/pmra) or contact the PMRA's Pest Management Information Service.

⁵ As per subsection 35(1) of the *Pest Control Products Act*.